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September 21, 1992

8EHQ-92-12479

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Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U. S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Sir or Madam:

Subject: Report submitted in accordance with guidelines established by the U. S. Environmental Protection Agency Registration and Agreement for the TSCA 8(e) Compliance Audit Program

Report submitted by: Eastman Kodak Company
343 State Street
Rochester, NY 14650
(716) 724-4000
CAP Agreement Identification Number (8ECAP-0039)

The report pertains to 5-chloro-3-nitro-1,2-benzenediamine [CAS # 42389-30-0] and is being submitted because of effects observed during a dermal sensitization study in guinea pigs. The test material was a moderate to strong sensitizer in all animals tested. The title of the report being submitted is "5-Chloro-3-nitro-1,2-benzenediamine Skin Sensitization Study (Footpad Method) in the Guinea Pig". The report is being identified as a study involving other than human effects (Unit II.B.2.b of CAP Agreement).

This compound is used internally and sold as a pure chemical. Annual sales have been 1 kg/year.

Questions regarding this submission should be addressed to:
Mr. William Hart, Eastman Kodak Company
Corporate Health and Environment Laboratories
Rochester, NY 14652-3615
(716) 722-5991

Sincerely,

R. Hays Bell

R. Hays Bell, Ph.D., Vice President
Corporate Health, Safety and Environment
(716) 722-5036

RECEIVED 3/9/95

RHB:JAF
Enclosure

STUDY TITLE

5-CHLORO-3-NITRO-1,2-BENZENEDIAMINE

SKIN SENSITIZATION STUDY (FOOTPAD METHOD) IN THE GUINEA PIG

FINAL REPORT

AUTHOR

Kenneth P. Shepard, B.S.

PERFORMING LABORATORY

Toxicological Sciences Laboratory
Health and Environment Laboratories
Eastman Kodak Company
1100 Ridgeway Avenue
B-320 Kodak Park
Rochester, New York 14652-3615
USA

STUDY SPONSOR

Eastman Kodak Company

STUDY COMPLETION DATE

December 19, 1990

Q.A. INSPECTION STATEMENT
(CFR 58.35(B)(7) 792.35(B)(7) 160.35(B)(7))

STUDY: 90-0155-1 STUDY DIRECTOR: TOPPING,D.C.
ACCESSION NUMBER: 905525

STUDY TYPE: SENSITIZATION

M. [signature] (AUDITOR, QUALITY ASSURANCE UNIT) 12/17/90 DATE

TO THE BEST OF MY KNOWLEDGE, THIS FINAL REPORT ACCURATELY DESCRIBES THE METHODS AND STANDARD OPERATING PROCEDURES, AND THE REPORTED RESULTS ACCURATELY REFLECT THE RAW DATA. THIS STUDY WAS INSPECTED BY 1 OR MORE PERSONS OF THE QUALITY ASSURANCE UNIT OF THE HAEL, EASTMAN KODAK COMPANY, ROCHESTER, N.Y. AND WRITTEN STATUS REPORTS WERE SUBMITTED ON THE FOLLOWING DATES:

INSPECTION DATES	PHASE(S) INSPECTED	STATUS REPORT DATES
11/12/90	PROTOCOL APPENDIX SUBMISSION IRRITATION INDUCTION	
11/19/90	TEST SYSTEM PREPARATION TEST ARTICLE DISTRIBUTION RECORDS TEST ARTICLE WEIGH AND MIX WITH CARRIER TEST ARTICLE DOSING OF TEST SYSTEM CHALLENGE	12/17/90
12/17/90	FINAL REPORT REVIEW	12/17/90

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

To the best of the signer's knowledge and belief, the study described by this report was conducted in compliance with the following Good Laboratory Practice Standards:

> Annex 2 of the Organization for Economic Cooperation and Development Guidelines for Testing of Chemicals C(81)30 (Final) as required by Council Directive 87/18/EEC of December 18, 1986.

Douglas C. Topping, Ph.D.
Study Director

December 19, 1990
Date

TABLE OF CONTENTS

STUDY TITLE

5-CHLORO-3-NITRO-1,2-BENZENEDIAMINE

SKIN SENSITIZATION STUDY (FOOTPAD METHOD) IN THE GUINEA PIG

ABSTRACT

A dermal sensitization study was conducted with 5-chloro-3-nitro-1,2-benzenediamine in guinea pigs using the footpad method. No signs of a dermal response were observed at challenge in any of the animals previously induced with Freund's adjuvant (control group). Moderate (4/10) to strong (6/10) erythema and slight edema (3/10) edema were observed at the application site on animals induced with the test material in Freund's adjuvant (test group) 24 hours after challenge. Only moderate (8/10) to strong (2/10) erythema was noted on test animals 48 hours after challenge. All animals survived to termination of the study and all gained weight normally.

Based on these results, the test material was considered to cause dermal sensitization in this strain of guinea pig when tested by the footpad method. These results indicate that the test material has a moderate potential for human dermal sensitization.

PERFORMING LABORATORY

Toxicological Sciences Laboratory
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Eastman Kodak Company
1100 Ridgeway Avenue
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Rochester, New York 14652-3615
USA

SPONSOR

Eastman Kodak Company

STUDY DATES

Study Initiation: November 12, 1990
Experiment Initiation: November 12, 1990
Experiment Completion: November 21, 1990
Study Completion: December 19, 1990

STUDY DIRECTOR

Douglas C. Topping, Ph.D., DABT

OTHER KEY PERSONNEL

John W. Mosher, B.S., and Chris M. Ashley, Study Technicians
Kenneth P. Shepard, B.S., Principal Investigator
Gordon J. Hankinson, D.V.M., M.S., Laboratory Animal Medicine

PURPOSE/OBJECTIVE

The purpose of the study was to determine whether the test material has the ability to produce delayed contact hypersensitivity (skin sensitization).

TEST SUBSTANCE

Chemical Name: 5-chloro-3-nitro-1,2-benzenediamine
CAS Registry Number: 042389-30-0
HAEL Laboratory Number: 90-0155
KAN: 905525
CIN: 10005525
SRID or Lot I.D. Number: ACA21507A
Physical State and Appearance: Brown solid
Received at Performing Laboratory: October 30, 1990
Composition: Refer to composition information included in the notification when applicable.

TEST SYSTEM

Species: Guinea Pig
Strain: Crl:(HA)BR VAF/Plus™
Source: Charles River Laboratories, Kingston, NY, USA
For Primary Irritation Screen:
No. of Animals: 5
Sex: Not determined
Body Weight Range: 475 - 554
Age: Not determined

For Induction and Challenge Study:
No. of Animals: 20; 10 control and 10 test animals
Sex: Male
Body Weight Range (g): 333 - 403
Age: Approximately 5-6 weeks old.

HUSBANDRY AND ENVIRONMENTAL CONDITIONS

Housing

All animals were individually housed in suspended stainless steel mesh cages.

Environmental Conditions

A photoperiod of 12 hours light from 6 a.m. to 6 p.m. was maintained. Room temperature was maintained at 70-72°F. Relative humidity was maintained at 34-36%.

Diet and Water

Agway® Prolab™ Guinea Pig Diet certified pellets, and water, obtained from the Monroe County (NY) Water Authority, were available ad libitum. No known contaminants which would interfere with the outcome of the study were expected to be present in feed or water from these sources. Analyses of feed and quarterly analyses of water are maintained on file within the testing laboratory.

HUSBANDRY AND ENVIRONMENTAL CONDITIONS CONT.

Isolation

Animals were isolated and monitored for at least five days after arrival and before release to the testing facility.

Animal Identification

All animals were identified by cage numbers and uniquely numbered metal ear tags.

TEST PROCEDURES AND CONDITIONS

Test Procedure Guideline

OECD Guideline for Testing of Chemicals: Guideline 406 (Annex), Dated 12 May, 1981.

Randomization

A clinical examination was performed on each animal to ensure that only healthy animals were utilized. The procedure for including animals in the study was to randomly select and assign animals from the same shipment to each group (test and control). Randomization was done by a computer-generated list using the Automated Animal Toxicology System. After assignment of animals to individual groups, the body weights were determined to ensure that all animals weighed between 300 and 500 grams at the initiation of the induction phase.

Identification Numbers of Animals Used

Primary irritation screen: 111 - 115

Sensitization study:
Induced with Freund's only (control group): 161 - 170
Induced with test material (test group): 171 - 180

Dosing Regimen and Evaluation

Primary Irritation Screen

Five animals, previously assigned as controls on a footpad sensitization study, were tested for primary skin irritation. Hair was removed from the backs of the animals with an electric clipper and 0.3 mL of a 1% solution of the test compound in a mixture of acetone, dioxane, and guinea pig fat (7:2:1) was applied to the clipped area. Twenty-four hours later the animals were depilated and scored for edema and erythema. The skin reaction was also scored at 48 hours. The highest average score for either day dictated the concentration to be used in the challenge dose of the main study.

TEST PROCEDURES AND CONDITIONS CONT.

Dosing Regimen and Evaluation Cont.

Primary Irritation Screen Cont.

The challenge dose was based on the following criteria. If the average was 0, a 10% solution was used for the challenge dose. If the average was 0.2 to 0.6, a 3% solution was used for the challenge dose. If the average was 0.8 to 1.2, a 1% solution was used for the challenge dose and if the average was 1.4 or more, a 0.1% solution was used.

Sensitization Procedure

Ten animals were injected in the footpad with 0.05 mL of Freund's complete adjuvant (control group). At the same time, 10 other animals were injected in the same manner with 0.05 mL of Freund's containing 1% test compound (test group). Seven days later the hair was removed from the backs of the animals with an electric clipper. The animals were then challenged with a solution of test material (at the concentration determined in the previous step) in acetone, dioxane, and guinea pig fat (7:2:1). The animals were depilated 24 hours after the challenge dose and the reaction to the topical challenge was scored. The next day (48 hours after challenge) the reaction was scored again.

Grading Sensitization Response

At both observation times, the challenged skin areas were graded for erythema and edema using numerical ratings as follows:

Erythema	Edema
0 - none	0 - none
1 - just discernible - slight	1 - just discernible to touch - slight
2 - easily determined - moderate	2 - easily determined - moderate
3 - dark red-strong	3 - difficult to pick up a fold of skin - strong

If an observation in the control group is greater than 2,0 (erythema, edema), the experiment may be repeated with a less concentrated solution. The response of each animal is interpreted as outlined below:

none:	1,0; 1,1; or 2,0 (see note below)
slight:	1,2; 2,1; or 3,0 (see note below)
moderate:	1,3; 2,2; or 3,1 (see note below)
strong:	2,3; 3,2; or 3,3

Note: A score of 2,0 is classified as no sensitization (none) if there is moderate or strong erythema in the control group. Otherwise, a score of 2,0 is considered evidence of slight sensitization. A score of 3,0 is classified as slight sensitization if there is moderate or strong erythema in the control group. Otherwise, a score of 3,0 is considered evidence of moderate sensitization.

TEST PROCEDURES AND CONDITIONS CONT.

Clinical Observations

Animals were observed once each day for mortality.

Body Weight Determinations

Body weights were collected on the day of the footpad induction and again when challenged.

Necropsy

Animals were not necropsied at the conclusion of the test.

RESULTS

Primary Irritation Screen

ANIMAL NUMBER	SCORE 24 HOURS	48 HOURS
111	0,0	0,0
112	0,0	0,0
113	0,0	0,0
114	0,0	0,0
115	0,0	0,0

The average score was 0. Therefore, the challenge concentration was set at 10%.

Sensitization Study

GROUP (CONTROL)	ANIMAL NUMBER	SCORE 24 HOURS	48 HOURS	GROUP (TEST)	ANIMAL NUMBER	SCORE 24 HOURS	48 HOURS
Freund's Complete Adjuvant Only	161	0,0	0,0	1% test material in Freund's Complete Adjuvant	171	2,0	2,0
	162	0,0	0,0		172	2,0	2,0
	163	0,0	0,0		173	3,0	2,0
	164	0,0	0,0		174	3,1	3,0
	165	0,0	0,0		175	2,0	2,0
	166	0,0	0,0		176	3,0	2,0
	167	0,0	0,0		177	3,0	2,0
	168	0,0	0,0		178	2,0	2,0
	169	0,0	0,0		179	3,1	3,0
	170	0,0	0,0		180	3,1	2,0

RESULTS CONT.

Description of Serious Lesions

No serious lesion was noted during the study.

Degree and Nature of Irritation

No dermal response was observed during the primary irritation screen. At challenge, no dermal response was observed for animals previously induced with Freund's adjuvant (control group). In animals previously induced with the test article in Freund's adjuvant (test group), responses seen 24 and/or 48 hours after challenge included moderate (4/10) to strong (6/10) erythema and slight edema (3/10).

Toxic Effects Other Than Irritation

No toxic effects or systemic clinical signs were noted during the study.

Weight Gain

All animals previously induced with Freund's adjuvant or the test material in Freund's adjuvant gained weight normally.

Individual Body Weights

GROUP (CONTROL)	ANIMAL NUMBER	BODY WEIGHTS (g) INITIAL	BODY WEIGHTS (g) END	GROUP (TEST)	ANIMAL NUMBER	BODY WEIGHTS (g) INITIAL	BODY WEIGHTS (g) END
Freund's Complete Adjuvant Only	161	362	402	1% test material in Freund's Complete Adjuvant	171	374	410
	162	385	434		172	333	387
	163	382	434		173	362	399
	164	390	462		174	381	431
	165	372	421		175	356	426
	166	371	430		176	397	465
	167	353	400		177	363	448
	168	352	410		178	376	441
	169	364	423		179	368	429
	170	403	476		180	382	460

DATA ANALYSIS

Evaluation of data was not done statistically, but rather by the following method.

The numbers of animals which were graded as having either a negative, slight, moderate, or strong sensitization response using the criteria outlined under Dosing Regimen and Evaluation were multiplied by the numerical values shown below.

Response Degree	Numerical Value
None	0
Slight	1
Moderate	5
Strong	10

The products of the multiplication were added together to obtain a total score. The estimated human risk potential for dermal sensitization is based on the total score of the test group. A total score of 0-9 is rated "low potential", 10-49 is rated "moderate potential", and 50-100 is rated "high potential".

DISCUSSION AND INTERPRETATION

No dermal response was observed during the primary irritation screen. No signs of a dermal response were observed at challenge for animals previously induced with Freund's adjuvant (control group). Moderate (4/10) to strong (6/10) erythema and slight edema (3/10) edema were observed at the application site on animals induced with the test material in Freund's adjuvant (test group) 24 hours after challenge. Only moderate (8/10) to strong (2/10) erythema was noted on the test animals 48 hours after challenge. All animals survived to termination of the study and all gained weight normally.

There was evidence that all ten test animals were sensitized. With a response of moderate erythema (2,0) representing a slight response for four animals; and strong erythema with no edema (3,0) or strong erythema with edema (3,1) representing a moderate response for six animals; the estimated human risk score was [(4x1) + (6x5)] = 34, indicating a moderate potential for human sensitization.

CONCLUSION

Based on these results, the test material was considered to cause dermal sensitization in this strain of guinea pig when tested by the footpad method. These results indicate that the test material has a moderate potential for human dermal sensitization.

DATA STORAGE

All test and control results presented in this report are supported by raw data which are maintained in the archives of the Health and Environment Laboratories, Eastman Kodak Company.

SIGNATURE PAGE

Kenneth P. Shapiro — December 6, 1990
Principal Investigator
Report Author — Date

David C. Jaggers — December 19, 1990
Director, Mammalian Toxicology Section
Study Director — Date

John [illegible] — December 19, 1990
Director, Toxicological Sciences Laboratory — Date

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

R. Hays Bell, Ph.D.
Vice President, Corporate Health, Safety, and Environment
Eastman Kodak Company
343 State Street
Rochester, New York 14650

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAY 0 8 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and **refer to the reverse side of this page for "EPA Information Requests"** .

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12479A

Triage of 8(e) Submissions

Date sent to triage: MAY [illegible]

NON-CAP CAP

Submission number: 12479A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

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entire document: 0 1 2 **pages** 1 **pages** 1, DNB

Notes:

Contractor reviewer : PDR **Date:** 4/26/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-0992-12479 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: Eastman Kodak Company

SUB. DATE: 09/21/92 OTS DATE: 09/24/92 CSRAD DATE: 03/09/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:

CAS#
42389-30-0

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
(0228)	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
(0248)	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA: NON-CBI INVENTORY
(YES)
CAS SR NO
(N TERMINI

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
GP

TOXICOLOGICAL CONCERN:
(LOW)
(MED)
HIGH

USE:
internal

PRODUCTION:
Sales 1 Kg/yr

COMMENTS

-CPSS- 0927952113

0 0 0 0 0 0 0 0 0 0 0 0
> <ID NUMBER>
8(e)-12479A

> <TOX CONCERN>
L/M

> <COMMENT>
SENSITIZATION IN GUINEA PIGS IS MEDIUM CONCERN. IN RESPONSE TO THE CHALLENGE DOSE OF A 10% SOLUTION: 6/10 EXHIBITED STRONG ERYTHEMA, 4/10 EXHIBITED MODERATE ERYTHEMA, AND 3/10 EXHIBITED SLIGHT EDEMA.

PRIMARY DERMAL IRRITATION IN GUINEA PIGS IS LOW CONCERN. THERE WERE NO POSITIVE RESPONSES WHEN 0.3 ML OF A 1% SOLUTION WAS APPLIED.

$$$$